REMARKS/ARGUMENTS

Claims 1, 6 and 7 were previously pending in the present application. Claims 8-16 were previously withdrawn. Claim 1 has been amended. No new matter has been added. Entry of the current amendment to claim 1 into the file of the present application is respectfully requested as it is believed to place the entire application in condition for an allowance or, at a minimum, to materially reduce the issues for an appeal.

Applicants acknowledge that the previous rejection under 35 U.S.C. § 101 has been withdrawn by the Examiner. Applicants further acknowledge and appreciate that the prior rejection under 35 U.S.C. § 112 has also been withdrawn by the Examiner in light of the previous response. Applicants address the Examiner's final remaining grounds for rejection below.

Claim Rejections Under 35 U.S.C. §103 (Non-Obviousness Requirement)

Claims 1, 6 and 7, directed to a system for incorporating unnatural amino acids into proteins in Eukaryotic translation in isolated animal host cells, have been rejected under 35 U.S.C. § 103(a) over Kiga et al.

In response to this rejection, previous claim 1 has been amended, without prejudice or disclaimer, to clarify that which Applicants deem to be the patentable subject matter of the present application. Claim 1 has been amended to clarify that the suppressor tRNA of the invention is a *B. stearothermophilus* suppressor tRNA and not intended to encompass *B. stearothermophilus* tRNA source sequences that have been manipulated to such a degree as to be identical, in fact, with suppressor tRNA sequences of *E. coli*, a profoundly distinct species (a species distant enough in sequence so as to be readily distinguishable and not subject to rendering "identical" through only very limited amino acid residue substitutions or other sequence modifications).

Applicants further note that as the tRNAs of the *B. Stearothermophilus* and *E. coli* species have diverged in their respective sequences through natural selection, so have the sequences of the corresponding suppressor tRNA and aminoacyl tRNA synthetases for each species (e.g., the native *E. coli* tyrosyl-tRNA synthetase sequence has but 56% identity to that of *B. stearothermophilus*). Thus, a scientist practicing in the field would understand that the sequence of the tRNA and the tRNA synthetase for each independent species would likely

coevolve together over time, but the same scientist would have no expectation that there would be any convergence between the sequences specific to the *B. stearothermophilus* suppressor tRNA (or tRNA synthetase) and those of the *E. coli* suppressor tRNA (or tRNA synthetase). Nor would such a scientist presume or reasonably expect an interchangeability or compatibility in functioning between the *B. stearothermophilus* suppressor tRNA with that of *E. Coli* suppressor tRNA, particularly with regard to association with the *E. coli* mutant tyrosyl-tRNA synthetase.

Recognizing the distinct sequences and properties of the *B. stearothermophilus* and *E. coli* suppressor tRNAs, respectively, and having no reasonable expectation that the suppressor tRNAs between species would be functionally compatible or equivalent, a scientist of average skill in the art would have no motivation to use a combination across these species, particularly a combination of the tRNA of *B. stearothermophilus* with the mutant tyrosyl-tRNA synthetase from *E. coli*, even in view of the Kiga reference teachings.

This lack of motivation is reinforced by the fact that *E. coli* tRNA synthetase coupled with *E. coli* suppressor tRNA (in both wild type and mutant form), when expressed in animal cells as per the present invention, failed to demonstrate suppression (and thus failed to perform the methods of the present invention). *See, e.g.*, pp. 48-51 and FIG. 4 of the present specification. Thus, even using the *E. coli* tRNA synthetase as an initial starting point for the present methods, let alone to combine the *E. coli* tRNA synthetase across species with a *B. stearothermophilus* suppressor tRNA, would be insufficiently motivated.

To the contrary, it is only by relying upon the disclosure contained in the present application that a scientist practicing in the field would recognize the value of and be motivated to practice the current methods as recited in claim 1. This holds true even as the present disclosure demonstrates suppression activity by the *B. stearothermophilus* suppressor tRNA associated with *E. coli* tRNA synthetase expressed in animal cells without alteration. While such cross-species findings are useful and are, in fact, important to the present invention, they were not readily predictable or to be reasonably expected prior to the teachings of the present disclosure.

Claim 1 as recited, along with pending claims 6 and 7 dependent thereto, is now believed to allay the concerns set forth by the examiner in the Office Action and to overcome the rejection under 35 U.S.C. § 103(a). Applicants respectfully ask that the examiner reconsider the

outstanding rejection under 35 U.S.C. § 103(a), in view of the amendments made to claim 1, and to deem that claims 1, 6 and 7 to be in suitable condition for prompt allowance.

Summary

This Amendment is believed to overcome all of the grounds for objection and rejection set forth in the August 7, 2008 Office Action regarding this application, which should therefore be withdrawn.

If the Examiner does not agree, however, but believes that an interview would advance the prosecution of this case, the Examiner is respectfully invited to telephone applicants' representative at the number below in order that an interview concerning this application may be scheduled.

Respectfully submitted,

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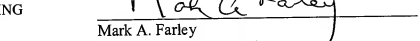

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